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To:

WATERMARK PATENT & TRADEMARK
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4 MAR 2004

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing
(day/month/year)

- 3 MAR 2004

Applicant's or agent's file reference

p21684pcau

REPLY DUE

within **TWO MONTHS**
from the above date of mailing

International Application No.

PCT/AU2003/000935

International Filing Date (day/month/year)

23 July 2003

Priority Date (day/month/year)

23 July 2002

International Patent Classification (IPC) or both national classification and IPC

Int. Cl. ⁷ C08G 18/32, 18/10, 18/77; C08K 3/32, 5/00; A61L 27/18, 27/58, 31/06

Applicant

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION et al

1. This written opinion is the **first** drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

3. The **FINAL DATE** by which the international preliminary examination report must be established according to Rule 69.2 is:
23 November 2004

4. The applicant is hereby **invited to reply** to this opinion.

When? See the **Reply Due** date indicated above. However, the Australian Patent Office will not establish the Report before the earlier of (i) a response being filed, or (ii) one month before the **Final Date** by which the international preliminary examination report must be established. The Report will take into account any response (including amendments) filed before the Report is established.
If no response is filed by 1 month before the Final Date, the international preliminary examination report will be established on the basis of this opinion.

Applicants wishing to have the benefit of a further opinion (if needed) before the report is established should ensure that a response is filed at least **3 months before the Final Date** by which the international preliminary examination report must be established.

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3.
For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4bis.
For an informal communication with the examiner, see Rule 66.6.

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I. Basis of the opinion**1. With regard to the elements of the international application:***

- ☒ the international application as originally filed.
- ☐ the description, pages , as originally filed,
 pages , filed with the demand,
 pages , received on with the letter of
- ☐ the claims, pages , as originally filed,
 pages , as amended under Article 19,
 pages , filed with the demand,
 pages , received on with the letter of
- ☐ the drawings, pages , as originally filed,
 pages , filed with the demand,
 pages , received on with the letter of
- ☐ the sequence listing part of the description:
 pages , as originally filed
 pages , filed with the demand
 pages , received on with the letter of

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/fig.

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"

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V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 8-9, 14-15, 17-21, 25	YES
	Claims 1-7, 10-13, 16, 22-24, 26-28	NO
Inventive step (IS)	Claims	YES
	Claims 1-28	NO
Industrial applicability (IA)	Claims 1-28	YES
	Claims	NO

2. Citations and explanations

The present application appears directed to biocompatible, biodegradable polymer compositions capable of in-vivo curing with low-heat generation (as well as ex-vivo curing) to form materials suitable as scaffolds in tissue engineering applications (eg, bone and cartilage repair).

The problem to solve appears to reside in providing biodegradable, biocompatible polymers capable of supporting living and non-living biological additives during preparation and use, which are also flowable and preferably injectable, in tissue engineering applications.

The following documents are considered relevant to the current application;

D1 - WO 1999/002168 A

D2 - Bruin et al, "Design and synthesis of biodegradable...." (3 May 1988)

D3 - Helminen et al, "Biodegradable crosslinked polymers..." (2001)

D4 - EP 0837084 A

D5 - US 5041516 A

D6 - WO 2002/010247 A

D7 - US 5886127 A

D8 - WO 2000/012579 A

D9 - US 5981684 A

D10 - US 2001/0005738 A

D11 - US 6376637 B

D1 discloses polymeric compositions (bioabsorbable) based on AB polyester polyether or related di-blocks (or ACA tri-blocks) suitable for use in medical applications (ie, biodegradable). Pages 3 and 25 disclose multi-block polymeric materials that comprise reaction products of C₂₋₂₄ diols (eg, polycaprolactone - OH terminated) and di-RNCO's which generate urethane groups in the polymers or di-NH₂'s and di-RNCO's (generating urea groups) - page 8. Page 16 discloses said polymers can be liquid polymers or gels (ie, 'flowable') which can be delivered to patients during surgery. Page 18 discloses said polymer compositions (either coupled di-blocks and soluble multi-blocks) are useful in producing crosslinked star or comb polymers. See also Page 33 and claims 32, 45, 58 and 71 of the cited reference. It is considered D1 anticipates at least claims 1-2, 4-7, 11-12 and 26-28.

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of V

D2 discloses PU network polymers derived from hexa-functional hydroxy (sugars) star-shaped polyester prepolymers that can be cross linked with lysine diisocyanate to produce non-toxic poly(ester-urethane) network polymer gels that are suitable for preparing degradable biomedical materials. It is considered that at least present claims 1-2, 4-5, 7 10-11, 16, 19, 22 and 26 are anticipated by the cited reference.

D3 discloses telechelic polylactide oligomers functionalised with alkoxysilanes (eg, IPTS) by urethane linkages and initiated with pentaerythritol. The oligomers are star-shaped and suitable as biodegradable, flowable (gels) biomedical materials (ie for use in bone cements and the like). Page 3347 (Col 2) discloses the steps taken to prepare said oligomers and particularly the second step depicts utilising an isocyanate to functionalise telechelic oligomers to form an intermediate branched prepolymer (star-shape). The reaction scheme on p3348 clearly discloses the urethane linkages after step two in the scheme prescribed on p3347 (Col 2). It is considered at least current claims 1-2, 4-5, 7, 11-12, 23 and 26-27 are anticipated by D3.

D4 discloses bioabsorbable branched polymers containing dioxanone units that can be advantageously end-capped with isocyanate and have a final product that is useful as medical or surgical devices or soft tissue wound healing applications (abstract and p3, lines 34-43). Said polymers are initiated with pentaerythritol which successfully controls the molecular weight of finished bioabsorbable polymer material. The polymers produced are star polymers and can be administered as an in-vivo implant or used as delivery vehicle for therapeutic agents by either diffusion or degradation. The polymers disclosed in D4 also appear to have 'flowability when used as cell growth substrates - see p5, (L38) to p7, (L39). It is considered at least current claims 1-2, 4-5, 7, 11-13, 23-24 and 26-28 are anticipated by D4.

Documents D5-D11 all disclose in one facet or another the subject matter of at least claims 1-7 and 26 of the present application. It would appear from the disclosure of these documents that star, dendritic or hyper-branched flowable polymer compositions comprising the reaction product of an isocyanate and low molecular weight multifunctional core molecules to produce urethane or urea linkages is well known. Accordingly the claims of the current application are anticipated by D5-D11 as set out below;

D5 anticipates present claims 1-2,4-5, 11 and 26

D6 anticipates present claims 1-7

D7 anticipates present claims 1-2, 4-5 and 26

D8 anticipates present claims 1-2 and 4-7

D9 anticipates present claims 1-5

D10 anticipates present claims 1-5

D11 anticipates present claims 1-2 and 4-6

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of V**NOVELTY (N) Claims 1-7, 10-13, 16, 22-24, 26-28**

Independent claim 1 merely defines a star, dendritic or hyper-branched prepolymer composition comprising urethane or urea linkages as the result of a reaction between any isocyanate and any low MW multifunctional core molecule able to react with NCO groups (functionality must be at least 2 or more groups on the core molecule) and having a viscosity that allows said composition to be flowable. The term 'flowable' is considered to encompass a viscosity of preferably 15000-200000 cSt at room temperature. Independent claim 26 defines a process to produce same under certain reaction conditions but said product is deemed biodegradable and biocompatible. In light of documents D1-D11 the subject matter of at least claims 1-7, 10-13, 16, 22-24 and 26-28 is considered anticipated by the cited documents.

INVENTIVE STEP (IS) Claims 1-28

Since D1-D11 anticipate the essential features of the present claims 1-7, 10-13, 16, 22-24 and 26-28, accordingly these claims are also considered to lack an inventive step in light of these references. It would appear the problem to solve in the current application is readily addressed in the cited documents.

Furthermore claims 8-9, 14-15, 17-21, 25 whilst being novel in light of D1-D11, it is considered these claims do not offer any further inventive features to the present invention, being standard known parameters in the art, and it would be obvious to a person skilled in the art to use such parameters at arriving at the solution to the problem encountered by the current application.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

- Page 17 of the description appears to have an inconsistency in the passages covering lines 12-15 of reaction scheme 1. The prepolymer prescribed therein does not appear to have any urethane or urea groups as claimed.
- Claim 5 of the current application appears to be incomplete. As a result present claim 5 is not clear in scope.

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